US 6,686,395 B2

119

120

| -continued | |
|------------|--|

| example No. | structure | MS (ES+): m/e = |
|----------------|-----------|--------------------|
| 18ai | | 494 |

Pharmacological Investigations

Kv1.5 channels from humans were expressed in Xenopus 20 oocytes. For this, oocytes from Xenopus laevis were first isolated and defolliculated. RNA encoding Kv1.5 synthesized in vitro was then injected into these oocytes. After Kv1.5 protein expression for 1-7 days, Kv1.5 currents were measured on the oocytes using the two-microelectrode voltage clamp technique. The Kv1.5 channels were in this case as a rule activated using voltage jumps to 0 mV and 40 mV lasting 500 ms. The bath was rinsed with a solution of the following composition: NaCl 96 mM, KCl 2 mM, CaCl₂ 1.8 mM, MgCl₂ 1 mM, HEPES 5 mM (titrated with NaOH to 30 pH 7.4). These experiments were carried out at room temperature. The following were employed for data acquisition and analysis: Geneclamp amplifier (Axon Instruments, Foster City, USA) and MacLab D/A converter and software (AD Instruments, Castle Hill, Australia). The substances according to the invention were tested by adding them in different concentrations to the bath solution. The effects of the substances were calculated as the percentage inhibition of the Kv1.5 control current which was obtained when no substance was added to the solution. The data were then extrapolated using the Hill equation in order to determine the inhibitory concentration IC50 for the respective sub-

The following IC₅₀ values were determined in this way for the compounds listed below:

| • | | | | | | | | |
|---|--------------------------|----------------|--------------------------|----------------|--------------------------|----------------|--------------------------|----------------|
| _ | IC _{so} [μΜ] | example No. | IC ₅₀ [μM] | example No. | IC _{so} [µM] | example No. | IC ₅₀ [μΜ] | example No. |
| | 3.0 | 6 h | 4.1 | 4 a | 2.6 | 2 a | 6.1 | 1 a |
| | ~6.0 | 7 a | 1.4 | 4 c | 0.8 | 2 Ь | 3.3 | 1 b |
| | 0.3 | 8 a | 1.8 | 4 d | 0.7 | 2 c | 1.0 | 1 d |
| | 0.9 | 8 b | 3.4 | 4 g | 1.7 | 2 d | 0.5 | 1 c |
| | 6.4 | 8 d | 1.8 | 4 h | 3.4 | 2 e | 0.4 | 1 f |
| | 4.5 | 8 j - | 4.7 | 4 i | 7.1 | 2 f | 0.4 | 1 g |
| | 3.1 | 8 k | 7.1 | 4 j | 3.3 | 2 g | 4.3 | 1 h |
| | 3.5 | 81 | 2.2 | 4 k | 2.5 | 2 h | 1.7 | 1 i |
| | 5.2 | 8 m | 0.8 | 41 | 3.3 | 2 i | 0.2 | 1 j |
| | 3.7 | 8 n | 4.5 | 5 a | 2.5 | 2 j | 2.4 | 1 k |
| | 8.4 | 8 0 | 7.8 | 5 c | 3.8 | 2 k | 1.4 | 11 |
| | 1.4 | 8 p | 1.9 | 5 d | 2.6 | 2 m | 0.7 | 1 m |
| | 7.3 | 8 q | 7.2 | 5 e | 1.7 | 3 d | 1.4 | 1 n |
| | 1.0 | 8 r | 4.4 | 6 a | 2.4 | 3 k | 4.4 | 1 o |
| | 1.0 | 8 s | 1.8 | 6 b | 2.6 | 31 | 0.8 | 1 r |
| | 3.3 | 8 x | 2.5 | 6 c | 1.9 | 3 p | 1.7 | 1 s |
| | 2.8 | 8 y | 3.1 | 6 d | 1.5 | 3 r | 1.3 | 1 t |
| | 1.6 | 8 z | 3.6 | 6 e | 3.0 | 3 | 0.8 | 1 u |
| | 3.0 | 9 Ъ | 1.1 | 8 ac | 1.2 | 8 ab | 0.8 | 8 aa |
| | 2.3 | 11 a | 2.2 | 9 g | 2.2 | 9 f | 2.0 | 9 c |

-continued

| example No. | ΙC ₅₀ [μΜ] | example No. | ΙC ₅₀ [μΜ] | example No. | ΙC ₅₀ [μΜ] | example No. | IC ₅₀ [μΜ] |
|----------------|--------------------------|----------------|--------------------------|----------------|--------------------------|----------------|--------------------------|
| 11 b | 7.3 | 11 d | 3.3 | 11 g | 7.8 | - 11 h | 5.8 |
| 11 I | 2.7 | 11 m | 3.3 | 11 n | 5.9 | 11 o | 4.4 |
| 11 p | 7.3 | 12 c | 11.2 | 12 f | 11.3 | 12 g | 9.1. |
| 12 h | 4.8 | 12 l | 10.3 | 12 m | 7.7 | 13 b | ~3.0 |
| 13 c | 1.4 | 13 d | 0.5 | 13 e | 2.8 | 13 f | 3.4 |
| 13 g | 1.1 | 13 h | 1.4 | 13 i | 1.2 | 14 a | 3.6 |
| 14 b | 2.7 | 14 d | 2.0 | 14 c | 0.8 | 14 f | 2.5 |
| 15 b | 3.1 | 16 b | 5.2 | 18 a | 7.2 | 18 b | 0.4 |
| 18 c | 4.2 | 18 d | 0.4 | 18 c | 1.7 | 18 f | 1.3 |
| 18 g | 3.9 | 18 h | 0.8 | 18 i | 0.4 | 18 j | 0.7 |
| 18 k | 3.0 | 18 m | 2.1 | 18 n | 0.4 | 18 o | 3.6 |
| 18 p | 4.7 | 18 q | 3.2 | 18 r | 0.7 | 18 s | 0.9 |
| 18 u | 1.1 | 18 v | 0.4 | 18 w | 5.4 | 18 x | 4.6 |
| 17 d | 1.3 | 17 e | 1.8 | 17 c | 2.1 | 18 y | 1.9 |
| 18 z | 1.2 | 18 aa | 0.4 | 18 ab | 1.1 | 18 ac | 10 |
| 18 ad | 0.3 | 18 af | 5.8 | 18 ah | 2.1 | 18 ai | 6.6 |

We claim:

1. A compound of the formula I,

$$R(5)$$
 $R(6)$ $R(4)$ $R(3)$ $R(3)$

in which:

R(1) is $SO_2R(10)$ or COR(11);

R(10) and R(11) are, independently of one another, defined as R(9)

R(9) is C_xH_{2x} —R(14); x is 0, 1, 2, 3 or 4

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 carbon atoms phenyl, naphthyl or biphenylyl,

where phenyl, naphthyl and biphenylyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

3. A compound as claimed in claim 2, in which:

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R(1) is SO_2R(10) or COR(11);
     or CF<sub>3</sub>;
                                                                          \hat{R}(9) is \hat{C}_x\hat{H}_{2x}—R(14); x is 0, 1, 2, 3 or 4,
  R(3) is C_yH_{2y}—R(16);
y is 0, 1, 2, 3 or 4,
                                                                             R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon
     R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 5
                                                                               atoms or phenyl,
       carbon atoms, phenyl or naphthyl,
                                                                                where phenyl is unsubstituted or substituted by 1
       where phenyl and naphthyl are unsubstituted or
                                                                                   or 2 substituents selected from the group con-
          substituted by 1, 2 or 3 substituents selected from
                                                                                   sisting of F, Cl, Br, CF<sub>3</sub>, OCF<sub>3</sub>, CN, COOMe,
          the group consisting of F, Cl, Br, I, CF<sub>3</sub>, OCF<sub>3</sub>, 10
                                                                                   CONH<sub>2</sub>, COMe, OH, alkyl having 1, 2 or 3
          NO2, CN, COOMe, CONH2, COMe, NH2, OH,
                                                                                   carbon atoms, alkoxy having 1 or 2 carbon
          alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy
                                                                                   atoms, dimethylamino, sulfamoyl, methylsul-
          having 1, 2, 3 or 4 carbon atoms, dimethylamino,
                                                                                   fonyl and methylsulfonylamino;
          sulfamoyl, methylsulfonyl and methylsulfony-
                                                                       R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms;
                                                                       R(3) is C_yH_{2y}—R(16);
y is 0, 1, 2, 3 or 4,
  R(4) is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon
     atoms or CF3;
                                                                          R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon
  R(5), R(6), R(7) and R(8)
                                                                             atoms or phenyl.
     independently of one another are hydrogen, F, Cl, Br, I,
                                                                             where phenyl is unsubstituted or substituted by 1 or
       CF<sub>3</sub>, NO<sub>2</sub>, CN, COOMe, CONH<sub>2</sub>, COMe, NH<sub>2</sub>, OH, 20
                                                                               2 substituents selected from the group consisting
       alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having
                                                                               of F, Cl, Br, CF<sub>3</sub>, OCF<sub>3</sub>, CN, COOMe, CONH<sub>2</sub>,
       1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl,
                                                                               COMe, NH<sub>2</sub>, OH, alkyl having 1, 2 or 3 carbon
       methylsulfonyl or methylsulfonylamino; and
                                                                               atoms, alkoxy having 1 or 2 carbon atoms,
                                                                               dimethylamino, sulfamoyl, methylsulfonyl and
                                                                               methylsulfonylamino;
     independently of one another are hydrogen or alkyl 25
                                                                       R(4) is hydrogen or alkyl having 1 or 2 carbon atoms;
       having 1, 2 or 3 carbon atoms;
                                                                       R(5), R(6), R(7) and R(8)
or a pharmaceutically acceptable salt thereof.
                                                                          independently of one another are hydrogen, F, Cl, Br,
  2. A compound as claimed in claim 1, in which
                                                                             CF<sub>3</sub>, CN, COOMe, CONH<sub>2</sub>, COMe, NH<sub>2</sub>, OH, alkyl
  R(1) is SO<sub>2</sub>R(10) or COR(11);
                                                                 30
                                                                             having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2
     R(9) is C_xH_{2x}-R(14);
                                                                             carbon atoms, dimethylamino, sulfamoyl, methylsul-
       x \text{ is } 0, 1, \overline{2}, 3 \text{ or } 4,
                                                                             fonyl or methylsulfonylamino; and
       R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon
                                                                       R(30) and R(31)
          atoms or phenyl,
                                                                          independently of one another are hydrogen or methyl.
           where phenyl is unsubstituted or substituted by 1, 35
                                                                        4. A compound as claimed in claim 3, in which:
              2 or 3 substituents selected from the group
                                                                       R(1) is SO<sub>2</sub>R(10) or COR(11);
              consisting of F, Cl, Br, CF<sub>3</sub>, OCF<sub>3</sub>, NO<sub>2</sub>, CN,
                                                                          R(9) is C_xH_{2x}-R(14);
              COOMe, CONH2, COMe, NH2, OH, alkyl
                                                                             x is 0, 1, \overline{2} or 3;
              having 1, 2, 3 or 4 carbon atoms, alkoxy having
                                                                             R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon
              1, 2, 3 or 4 carbon atoms, dimethylamino, 40
                                                                               atoms or phenyl,
             sulfamoyl, methylsulfonyl and methylsulfony-
                                                                                where phenyl is unsubstituted or substituted by 1
              lamino:
                                                                                   or 2 substituents selected from the group con-
  R(2) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms
                                                                                   sisting of F, Cl, CF<sub>3</sub>, OCF<sub>3</sub>, OH, alkyl having
     or CF<sub>3</sub>;
                                                                                   1, 2 or 3 carbon atoms and alkoxy having 1 or
  R(3) is C<sub>y</sub>H<sub>2y</sub>—R(16);
y is 0, 1, 2, 3 or 4,
                                                                                   2 carbon atoms;
                                                                       R(2) is hydrogen;
     R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon
                                                                       R(3) is C_v H_{2v} - R(16);
       atoms or phenyl,
                                                                          y is 0, 1 or 2;
        where phenyl is unsubstituted or substituted by 1, 2
                                                                          R(16) is cycloalkyl having 5 or 6 carbon atoms or
          or 3 substituents selected from the group consist-
          ing of F, Cl, Br, CF<sub>3</sub>, OCF<sub>3</sub>, NO<sub>2</sub>, CN, COOMe,
                                                                             where phenyl is unsubstituted or substituted by 1 or
          CONH<sub>2</sub>, COMe, NH<sub>2</sub>, OH, alkyl having 1, 2, 3 or
                                                                               2 substituents selected from the group consisting
          4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon
                                                                               of F, Cl, CF<sub>3</sub>, OCF<sub>3</sub>, OH, alkyl having 1, 2 or 3
          atoms, dimethylamino, sulfamoyl, methylsulfonyl
                                                                               carbon atoms and alkoxy having 1 or 2 carbon
           and methylsulfonylamino;
                                                                                atoms:
  R(4) is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon
                                                                       R(4) is hydrogen; and
     atoms or CF3; and
                                                                       R(5), R(6), R(7) and R(8)
                                                                          independently of one another are hydrogen, F, CF<sub>3</sub>,
   R(5), R(6), R(7) and R(8)
     independently of one another are hydrogen, F, Cl, Br, 60
                                                                             CN, COOMe, CONH2, NH2, OH, alkyl having 1, 2
                                                                             or 3 carbon atoms or alkoxy having 1 or 2 carbon
        CF<sub>3</sub>, NO<sub>2</sub>, CN, COOMe, CONH<sub>2</sub>, COMe, NH<sub>2</sub>, OH,
        alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having
                                                                             atoms; and
        1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl,
                                                                        R(30) and R(31)
        methylsulfonyl or methylsulfonylamino; and
                                                                          independently of one another are hydrogen or methyl.
                                                                        5. A compound as claimed in claim 4, in which:
  R(30) and R(31)
     independently of one another are hydrogen or alkyl
                                                                        R(1) is COR(11);
                                                                          R(9) is C_xH_{2x}--R(14);
       having 1, 2 or 3 carbon atoms.
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x is 0, 1, 2 or 3;

R(14) is cycloalkyl having 5 or 6 carbon atoms or phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(2) is hydrogen;

R(3) is C_yH_{2y} —R(16);

y is 0, 1 or 2;

R(16) is cycloalkyl having 5 or 6 carbon atoms or phenyl

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(4) is hydrogen; and

R(5), R(6), R(7) and R(8)

independently of one another are hydrogen, F, CF₃, alkyl having 1, 2 or 3 carbon atoms or alkoxy having 1 or 2 carbon atoms; and

R(30) and R(31)

are hydrogen.

- 6. A pharmaceutical composition, comprising an effective amount of at least one compound as claimed in claim 1 together with a pharmaceutically acceptable vehicle or additive.
- 7. A method for the therapy of a K⁺ channel-mediated 30 illness, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
- 8. A method for the therapy of a cardiac arrythmia which can be eliminated by action potential prolongation, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
- 9. A method for the therapy of a re-entry arrythmia, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
- 10. A method for the therapy of a supraventricular arrythmia, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
- 11. A method for the therapy of atrial fibrillation or atrial flutter, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
- 12. A method for terminating existing atrial fibrillation or flutter to restore sinus rhythm, which comprises administering to a host in need of the termination an effective amount of a compound as claimed in claim 1.

13. A compound as claimed in claim 1, in which:

R(1) is $SO_2R(10)$ or COR(11);

R(9) is $C_xH_{2x}-R(14)$;

x is 0, 1, 2, 3 or 4.

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl.

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms; R(3) is C_vH_{2v} —R(16); y is 0, 1, 2, 3 or 4,

R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon

atoms or phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4) is hydrogen or alkyl having 1 or 2 carbon atoms;

R(5), R(6), R(7) and R(8)

independently of one another are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino; and

R(30) and R(31)

independently of one another are hydrogen or methyl. 14. A compound as claimed in claim 1, in which

R(30) and R(31) are both hydrogen;

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 carbon atoms, phenyl, naphthyl or biphenylyl,

where phenyl, naphthyl and biphenylyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOMe, CONIL₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11

carbon atoms, phenyl or naphthyl,

where phenyl and naphthyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.

15. A compound as claimed in claim 2, in which

R(30) and R(31) are both hydrogen;

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon

atoms or phenyl,

where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon

atoms or phenyl,

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where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.

16. A compound as claimed in claim 3, in which:

R(30) and R(31) are both hydrogen;

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms or phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substitutents selected from the group consisting of F,

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Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(16) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon ⁵ atoms or phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.

17. A compound as claimed in claim 4, in which:

R(30) and R(31) are both hydrogen;

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon

atoms or phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(16) is cycloalkyl having 5 or 6 carbon atoms or phenyl,

where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms.

18. A compound as claimed in claim 5, in which:

R(14) is cycloalkyl having 5 or 6 carbon atoms or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(16) is cycloalkyl having 5 or 6 carbon atoms or phenyl where phenyl is unsubstituted or substituted by 1 or 2 substitutents selected from the group consisting of F, Cl, CF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms.

19. A method for preventing the re-occurrence of arrhythmias, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.

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The following IC₅₀ values were determined in this way for the compounds listed below:

| example No. | IC ₅₀ [μΜ] | example No. | IC ₅₀ example $[\mu M]$ No. | IC _{so} example [μΜ] No. | IC _{so} [μΜ] |
|----------------|--------------------------|----------------|--|--------------------------------------|--------------------------|
| 1a | 6.1 | 2a | 2.6 4a | 4.1 6h | 3.0 |
| 1b | 3.3 | 2b | 0.8 4c | 1.4 7a | ~6.0 |
| 1d | 1.0 | 2c | 0.7 4d | 1.8 8a | 0.3 |
| 1e | 0.5 | 2d | 1.7 4g | 3.4 8b | 0.9 |
| 1f | 0.4 | 2e | 3.4 4h | 1.8 8d | 6.4 |
| 1g | 0.4 | 2 f | 7.1 4i | 4.7 8j | 4.5 |
| 1ĥ | 4.3 | 2g | 3.3 4j | 7.1 8k | 3.1 |
| 1i | 1.7 | 2h | 2.5 4k | 2.2 81 | 3.5 |
| 1j | 0.2 | 2i | 3.3 41 | 0.8 8m | 5.2 |
| 1k | 2.4 | 2j | 2.5 5a | 4.5 8n | 3.7 |
| 11 | 1.4 | 2k | 3.8 5c | 7.8 8o | 8.4 |
| 1m | 0.7 | 2m | 2.6 5d | 1.9 8p | 1.4 |
| 1n | 1.4 | 3d | 1.7 5e | 7.2 8q | 7.3 |
| 1o | 4.4 | 3k | 2.4 6a | 4.4 8r | 1.0 |
| 1r | 0.8 | 31 | 2.6 6b | 1.8 8s | 1.0 |
| 1s | 1.7 | 3p | 1.9 6c | 2.5 8x | 3.3 |
| 1t | 1.3 | 3r | 1.5 6d | 3.1 8y | 2.8 |
| 1u | 0.8 | 3 | 3.0 6e | 3.6 8z | 1.6 |
| 8aa | 0.8 | 8ab | 1.2 8ac | 1.1 9b | 3.0 |
| 9c | 2.0 | 9f | 2.2 9g | 2.2 11a | 2.3 |
| 11b | 7.3 | 11d | 3.3 11g | 7.8 11h | 5.8 |
| 11l | 2.7 | 11 m | 3.3 11n | 5.9 11o | 4.4 |
| 11p | 7.3 | 12c | 11.2 12f | 11.3 12g | 9.1 |
| 12h | 4.8 | 121 | 10.3 12m | 7.7 13b | ~3.0 |
| 13c | 1.4 | 13d | 0.5 13e | 2.8 13f | 3.4 |
| 13g | 1.1 | 13h | 1.4 13i | 1.2 14a | 3.6 |
| 14b | 2.7 | 14d | 2.0 14c | 0.8 14f | 2.5 |
| 15b | 3.1 | 16b | 5.2 18a | 7.2 18b | 0.4 |
| 18c | 4.2 | 18d | 0.4 18e | 1.7 18f | 1.3 |
| 18g | 3.9 | 18h | 0.8 18i | 0.4 18 | 0.7 |
| 18k | 3.0 | 18m | 2.1 18n | 0.4 180 | 3.6 |
| 18p | 4.7 | 18q | 3.2 18r | 0.7 18s | 0.9 |
| 18u | 1.1 | 18v | 0.4 18w | 5.4 18x | 4.6 |
| 17d | 1.3 | 17e | 1.8 17c | 2.1 18y | 1.9 |
| 18z | 1.2 | 18aa | 0.4 18ab | 1.1 18ac | 10 |
| 18ad | 0.3 | 18af | 5.8 18ah | 2.1 18ai | 6.6 |

We claim:

1. A compound of the formula I,

$$R(5)$$
 $R(6)$
 $R(4)$
 $R(30)$
 $R(31)$
 $R(3)$
 $R(3)$

in which:

R(1) is C(0)OR(9), $SO_2R(10)$, COR(11), C(0)NR(12)R(13) or C(S)NR(12)R(13);

R(9) is C_1H_{2x} —R(14); x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is OR(15) or SO₂Me;

R(14) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 60 carbon atoms, CF₃, C₂F₅, C₃F₇, CH₂F, CHF₂, OR(15), SO₂Me, phenyl, naphthyl or biphenylyl, where phenyl, naphthyl and biphenylyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, 65 CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms,

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alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF3 or phenyl which is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino:

R(10), R(11) and R(12) independently of one another are defined as R(9):

R(13) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF₃;

R(2) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF₃;

R(3) is C_yH_{2y} —R(16); y is 0, 1, 2, 3 or 4, where y cannot be 0 if R(16) is OR(17) or SO₂Me;

R(16) is OR(17) or a six membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, OCF₃, NO₂, ČN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; or

R(3) is CHR(18)R(19);

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R(18) is $C_zH_{2z}-R(16)$, where R(16) is defined as indicated above;

z is 0, 1, 2 or 3;

R(19) is COOH, CONH2, CONR(20)R(21), COOR (22), or CH₂OH;

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C,H2,-CF3 or C,H2,-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substitutents selected from the group consisting of F, Cl, Br, I, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or

4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3;

w is 0, 1, 2 or 3;

R(21) is hydrogen or alkyl having 1, 2, 3, 4 or 5 carbon atoms:

R(22) is alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(4) is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or CF₃;

R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, I, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms,

dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;

R(30) and R(31) independently of one another are hydrogen or alkyl having 1, 2 or 3 carbon atoms; or

R(30) and R(31) together form a chain of 2 methylene 5 groups;

or a pharmaceutically acceptable salt thereof.

2. A compound as claimed in claim 1, in which R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12) R(13);

R(9) is C_xH_{2x} —R(14),

x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is OR(15);

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, C₂F₅, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1, 2, 3, 4 or 5 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF₃ or phenyl, which is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.

R(10), R(11) and R(12) independently of one another are defined as R(9);

R(13) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF₃;

R(2) is hydrogen, alkyl having 1, 2, 3 or 4 carbon atoms or CF₃;

R(3) is $C_yH_{2y}--R(16)$;

y is 0, 1, 2, 3 or 4, where y cannot be 0 if R(16) is OR(17);

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, 50 methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3-, or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substitutents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, 55 COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; or

R(3) is CHR(18)R(19);

R(18) is C_zH_{2z}—R(16), where R(16) is defined as indicated in claim 1 above;

z is 0, 1, 2 or 3;

R(19) is CONH₂, CONR(20)R(21), COOR(22), CH₂OH;

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, $C_\nu H_{2\nu}$ — CF_3 or $C_\nu H_{2\nu}$ -phenyl, where the

phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3;

w is 0, 1, 2 or 3;

R(21) is hydrogen or alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(22) is alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(4) is hydrogen, alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms or CF₃; and

R(5), R(6), R(7) and R(8) independently of one another are hydrógen, F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;

R(30) and R(31) independently of one another are hydrogen or alkyl having 1, 2 or 3 carbon atoms; or

R(30) and R(31) together form a chain of 2 methylene groups.

3. A compound as claimed in claim 2, in which:

R(1) is C(O)OR(9), $SO_2R(10)$, COR(11) or C(O)NR(12) R(13);

R(9) is $C_xH_{2x}-R(14)$;

x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is OR(15);

R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1 or 2 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF₃ or phenyl, which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(10), R(11) and R(12) independently of one another are defined as R(9);

R(13) is hydrogen;

R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms; R(3) is CHR(18)R(19);

R(18) is $C_2H_{2z}-R(16)$;

z is 0, 1, 2 or 3;

R(19) is CONH₂, CONR(20)R(21), COOR(22) or CH₂OH;

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C_vH_{2v}—CF₃ or C_wH_{2w}-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3; w is 0, 1, 2 or 3;

R(21) is hydrogen or alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(22) is alkyl having 1, 2, 3, 4 or 5 carbon atoms; 5 R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substitutents selected from the group consisting of F, Cl, Br, 10 CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 20 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4) is hydrogen or alkyl having 1 or 2 carbon atoms; and R(5), R(6), R(7) and R(8) independently of one another ²⁵ are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;

R(30) and R(31) independently of one another are hydrogen or methyl; or

R(30) and R(31) together form a chain of 2 methylene groups.

4. A compound as claimed in claim 2, in which:

R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12) R(13):

R(9) is C_xH_{2x} —R(14);

x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is OR(15);

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected fro m the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1 or 2 carbon atoms, 50 cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF₃ or phenyl, which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 55 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(10), R(11) and R(12) independently of one another are defined as R(9);

R(13) is hydrogen;

R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms; R(3) is C.H. -R(16):

R(3) is C_yH_{2y}—R(16); y is 0, 1, 2, 3 or 4, where y cannot be 0 if R(16) is OR(17);

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom,

where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substitutents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4) is hydrogen or alkyl having 1 or 2 carbon atoms;

R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;

R(30) and R(31) independently of one another are hydrogen or methyl; or

R(30) and R(31) together form a chain of 2 methylene groups.

5. A compound as claimed in claim 4, in which:

R(1) is C(0)OR(9), SO₂R(10), COR(11) or C(0)NR(12) R(13);

R(9) is C_xH_{2x} —R(14); x is 0, 1, 2 or 3;

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃ or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(10), R(11) and R(12) independently of one another are defined as R(9);

R(13) is hydrogen;

R(2) is hydrogen;

R(3) is $C_v H_{2v} - R(16)$;

y is 0, 1 or 2;

R(16) is pyridyl, where pyridyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms;

R(4) is hydrogen; and

R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, CF₃, CN, COOMe, CONH₂, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms or alkoxy having 1 or 2 carbon atoms;

R(30) and R(31) independently of one another are hydrogen or methyl; or

R(30) and R(31) together form a chain of 2 methylene groups.

6. A compound as claimed in claim 5, in which:

R(1) is C(0)OR(9) or COR(11);

R(9) is C_xH_{2x} —R(14);

x is 0, 1, 2 or 3;

R(14) is cycloalkyl having 5 or 6 carbon atoms or phenyl, where phenyl is unsubstituted or substi 5

tuted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, alkyl having 1, 2 or 3 carbon ato ms and alkoxy having 1 or 2 carbon atoms;

R(11) is defined as R(9);

R(2) is hydrogen;

R(3) is C_yH_{2y} —R(16);

y is 0, 1 or 2;

R(16) is pyridyl where pyridyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OCF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms:

R(4) is hydrogen; and

R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, CF₃, alkyl having 1, 2 or 3 carbon atoms or alkoxy having 1 or 2 carbon atoms;

R(30) and R(31) are hydrogen.

- 7. A pharmaceutical composition, comprising an effective 20 amount of at least one compound as claimed in claim 1 together with a pharmaceutically acceptable vehicle or additive.
- 8. A pharmaceutical composition as claimed in claim 7, which further comprises one or more other pharmacologi- 25 cally active compounds.
- 9. A method for the therapy of a K⁺ channel-mediated illness, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
- 10. A method for the therapy of a cardiac arrythmia which can be eliminated by action potential prolongation, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
- 11. A method for the therapy of a re-entry arrythmia, 35 which comprises administering to a host in need of the therapy an effective amount of a compound as claimed in claim 1.
- 12. A method for the therapy of a supraventricular arrythmia, which comprises administering to a host in need 40 of the therapy an effective amount of a compound as claimed in claim 1.
- 13. A method for the therapy of atrial fibrillation or atrial flutter, which comprises administering to a host in need of the therapy an effective amount of a compound as claimed 45 in claim 1.
- 14. A method for terminating existing atrial fibrillation or flutter to restore sinus rhythm, which comprises administering to a host in need of the termination an effective amount of a compound as claimed in claim 1.
- 15. A pharmaceutical composition as claimed in claim 7, which further comprises an effective amount of an IKr channel blocker.
- 16. A pharmaceutical composition as claimed in claim 7, which further comprises an effective amount of an IKs 55 channel blocker.
- 17. A pharmaceutical composition as claimed in claim 7, which further comprises an effective amount of a beta-blocker.
 - 18. A compound as claimed in claim 1, in which:
 - R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12) R(13);

R(9) is $C_xH_{2x}-R(14)$;

- x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is OR(15);
- R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is

unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1 or 2 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms, CF₃ or phenyl, which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(10), R(11) and R(12) independently of one another are defined as R(9);

R(13) is hydrogen;

R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms; R(3) is CHR(18)R(19);

R(18) is $C_zH_{2z}--R(16)$;

z is 0, 1, 2 or 3;

R(19) is CONH₂, CONR(20)R(21), COOR(22) or CH₂OH;

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C_vH_{2v}—CF₃ or C_wH_{2w}-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3;

w is 0, 1, 2 or 3;

R(21) is hydrogen or alkyl having 1, 2, 3, 4 or 5 carbon atoms;

R(22) is alkyl having 1, 2, 3, 4 or 5 carbon atoms; R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substitutents selec ted from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4) is hydrogen or alkyl having 1 or 2 carbon atoms; and R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;

R(30) and R(31) independently of one another are hydrogen or methyl; or

R(30) and R(31) together form a chain of 2 methylene groups.

19. A compound as claimed in claim 1, in which:

R(1) is C(O)OR(9), SO₂R(10), COR(11) or C(O)NR(12) R(13);

R(9) is $C_xH_{2x}-R(14)$;

x is 0, 1, 2, 3 or 4, where x cannot be 0 if R(14) is 5 OR(15);

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents 10 selected from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(15) is alkyl having 1 or 2 carbon atoms, cycloalkyl having 3, 4, 5 or 6 carbon atoms. CF3 or phenyl, which is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, ²⁰ COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(10), R(11) and R(12) independently of one another 25 are defined as R(9);

R(13) is hydrogen;

R(2) is hydrogen or alkyl having 1, 2 or 3 carbon atoms; R(3) is C_yH_{2y}—R(16); y is 0, 1, 2, 3 or 4, where y cannot be 0 if R(16) is ³⁰

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substituents selected 35 from the group consisting of F, Cl, Br, CF₃, OCF₃, CN, COOMe, CONH2, COMe, NH2, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, OCF₃, NO₂, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(4) is hydrogen or alkyl having 1 or 2 carbon atoms;

R(5), R(6), R(7) and R(8) independently of one another are hydrogen, F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl or methylsulfonylamino;

R(30) and R(31) independently of one another are hydrogen or methyl; or

R(30) and R(31) together form a chain of 2 methylene

20. A compound as claimed in claim 1, in which R(30) and R(31) are both hydrogen;

R(14) is alkyl having 1, 2, 3, 4, 5 or 6 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8, 9, 10 or 11 carbon atoms, CF₃, C₂F₅, C₃F₇, CH₂F, CHF₂, OR(15), SO₂Me, phenyl, naphthyl or biphenylyl, where phenyl, 65 naphthyl an d biphenylyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group

consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOMe, CONH2, COMe, NH2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, I, CF₃, NO2, CN, COOMe, CONH2, COMe, NH2, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, meth-

ylsulfonyl and methylsulfonylamino; and

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C_vH_{2v}--CF₃ or C_wH_{2w}-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substitutents selected from the group consisting of F, Cl, Br, I, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms. dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3; w is 0, 1, 2 or 3.

21. A compound as claimed in claim 2, in which R(30) and R(31) are both hydrogen;

R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, C₂F₅, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

R(17) is 2-, 3-, or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO2, CN, COOMe, CONH2, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; and

R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C,H_{2v}—CF₃ or C_wH_{2w}-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO₂, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;

v is 0, 1, 2 or 3; w is 0, 1, 2 or 3.

- 22. A compound as claimed in claim 3, in which R(30) and R(31) are both hydrogen;
- R(14) is cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, 10 dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- R(20) is hydrogen, alkyl having 1, 2, 3, 4 or 5 carbon atoms, C,H2,-CF3 or C,H2,-phenyl, where the phenyl ring is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; v is 0, 1, 2 or 3;

w is 0, 1, 2 or 3;

- R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, 25 where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substitutents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino; and
- R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl is unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, 35 CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.
- 23. A compound as claimed in claim 4, in which R(30) and R(31) are both hydrogen;
- R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃, OR(15) or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consist-

- ing of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- R(16) is OR(17) or a six-membered N-containing heteroaromatic having 5 carbon atoms and one N-atom, where the N-containing heteroaromatic is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, Br, CF₃, CN, COOMe, CONH₂, COMe, NH₂, OH, alkyl having 1, 2 or 3 carbon atoms, alkoxy having 1 or 2 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino;
- R(17) is 2-, 3- or 4-pyridyl, where 2-, 3- or 4-pyridyl are unsubstituted or substituted by 1, 2 or 3 substituents selected from the group consisting of F, Cl, Br, CF₃, NO2, CN, COOMe, CONH2, COMe, OH, alkyl having 1, 2, 3 or 4 carbon atoms, alkoxy having 1, 2, 3 or 4 carbon atoms, dimethylamino, sulfamoyl, methylsulfonyl and methylsulfonylamino.
- 24. A compound as claimed in claim 5, in which

R(30) and R(31) are both hydrogen;

- R(14) is alkyl having 1, 2, 3 or 4 carbon atoms, cycloalkyl having 3, 4, 5, 6, 7, 8 or 9 carbon atoms, CF₃ or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms; and
- R(16) is pyridyl, where pyridyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, OH, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms. 25. A compound as claimed in claim 6, in which
- R(14) is cycloalkyl having 5 or 6 carbon atoms or phenyl, where phenyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms; and
- R(16) is pyridyl where pyridyl is unsubstituted or substituted by 1 or 2 substituents selected from the group consisting of F, Cl, CF₃, alkyl having 1, 2 or 3 carbon atoms and alkoxy having 1 or 2 carbon atoms.